REMARKS

In the Office Action, claims 10-18 and 26-30 have been withdrawn from further consideration as allegedly being drawn to a non-elected invention; claims 1-9 and 19-25 are rejected under 35 U.S.C §112, first paragraph; claims 1-9 and 19-25 are rejected under 35 U.S.C. §112, second paragraph; and claims 1-9 and 19-25 are rejected under 35 U.S.C. §103. Claims 1, 5, 9, 10, 13 19, 23, 24, and 25 have been amended; and claims 4, 6, 8, 11, 12, 18, 21, and 22 have been cancelled without prejudice or disclaimer. Applicants believe that the rejections have been overcome in view of the amendments and at least for the reasons set forth below.

At the outset, claims 10-18 and 26-30 have been withdrawn from further consideration as allegedly drawn to a non-elected invention as previously discussed. Applicants respectfully request reconsideration at least with respect to the non-election of claims 10-18. As previously provided, independent claim 10 has been amended to include in part that the reagent is derived from a silkworm larvae plasma and that the threshold level of peptidoglycan in the peritoneal dialysis solution is about 10ng/mL or less so as to prevent peritonitis in the patient. These changes are consistent with changes made to independent claims 1 and 19 of the elected subject matter, and thus, further support Applicants' position that the claims of alleged Groups I and II cover similar subject matter. Therefore, Applicants once again request that claims 10-18 be considered for examination purposes along with claims 1-9 and 19-25. Of these claims, claims 4, 6, 8, 11, 12, 18, 21, and 22 have been cancelled without prejudice or disclaimer as previously discussed.

Claims 1-9 and 19-25 have been rejected under 35 U.S.C. §112, first and second paragraphs. In response, Applicants have amended some of the claims and canceled others without prejudice or disclaimer as discussed above. Therefore, Applicants believe that the pending claims satisfy the requirements pursuant to 35 U.S.C. §112. Accordingly, Applicants respectfully request that the rejections pursuant to 35 U.S.C. §112 be withdrawn.

In the Office Action, claims 1-9 and 19-25 are rejected under 35 U.S.C. §103 in view of Gokal et al; Martin et al; and Goffin et al, each in view of Tsuchiya et al, and further in view of Ashida et al. Applicants believe that this rejection has been overcome and thus should be withdrawn.

Of the pending claims at issue, claims 1 and 19 are the sole independent claims and have been amended as previously provided. The inventors have surprisingly discovered a novel cause of aseptic peritonitis – aseptic peritonitis associated with gram positive microbial contamination of a dialysis solution. Peptidoglycan is a major component of a gram positive bacterial cell wall and thus can serve as a marker for gram positive bacteria. In this regard, screening for peptidoglycan contamination associated with the peritoneal dialysis solution can be effectively utilized to prevent peritonitis in patients that use the peritoneal dialysis solutions, such as peritoneal dialysis solutions that contain a glucose polymer including an icodextrin powder. See, Specification, page 10, lines 7-14.

Icodextrin and the like is derived from corn starch, a natural product. It is known that products of natural origin are contaminated with a wide variety of micro-organisms. The inventors have found that some natural products, such as corn starch, contain an acidophilic thermophilic bacteria, such as Alicyclobacillus acidocaldariuos. See, Specification, page 6, lines 24-27. Peritoneal dialysis solutions and parenteral solutions in general have not been recognized to have been contaminated by this type of organism or its degradation products. This is mainly because the current testing procedure for microbial contamination of peritoneal dialysis solutions and parenteral solutions in general are not capable of detecting this organism or its degradation products. See, Specification, page 7, lines 3-7.

Bacterial cultures are generally performed at neutral pH using an incubation temperature between 20-35°C. These are suboptimal conditions for the growth of thermophilic acidophilic microorganisms including Alicyclobacillus acidocaldariuos that require and acid medium and elevated temperature for growth. Therefore, routinely employed "sterility definitions" and the supporting assays may fail to detect microrgansims that do not grow under conventional conditions. See, Specification, page 12, lines 3-11.

Because the manufacture of icodextrin from maltodextrin requires heat and acidification, a microbiological investigation was conducted for the presence of acidophilic thermophilic bacteria, such as Alicyclobacillus acidocaldariuos, in the icodextrin batch. Early steps of the icodextrin were found to be contaminated with such bacteria that was further determined to be the source of the contaminating peptidoglycan. Heat and sterile procedures applied to the near final product eliminated the bacteria, but not the peptidoglycan contaminants. A positive

correlation was found between peptidoglycan levels in icodextrin and the IL-6 response observed in the PBMC assay. See, Specification, page 17, lines 19-28. Based on these and further investigations, Applicants have found that testing for peptidoglycan (e.g., SLP test) and acidophilic thermophilic bacteria (e.g., modified bioburden test) associated with the glucose polymer (e.g., icodextrin raw material) can be used to determine whether a solution that contains the glucose polymer can be made at peptidoglycan levels that do not exceed 10 ng/mL and further whether the solution is sterile. At or below this peptidoglycan threshold level, the inventors have determined that a peritoneal dialysis solution can be made without causing peritonitis due to peptidoglycan contamination during use of same. See, Specification, for example, pages 14-19.

The Patent Office primarily relies on the Gokal et al, Martin et al and Goffin et al references in support of the obviousness rejection. Yet, the references fail to report a threshold level of peptidoglycan that can be tolerated in the peritoneal dialysis solution as even admitted by the Patent Office (See, Office Action, page 10) in contrast to the claimed invention. To support the deficiencies of these references, the Patent Office further alleges that one of ordinary skill in the art would have been motivated to determine the concentration of the peptidoglycan present in contaminated samples of icodextrin in order to determine if a level is low enough for safe distribution and further one would have expected success in quantifying the concentration of peptidoglycan in the solution based on the alleged teaching of Ashida.

Yet, nowhere does Ashida disclose or suggest that peptidoglycan in glucose polymer-based peritoneal dialysis solutions, let alone at amounts that exceed 10 ng/mL, was the causative agent of aseptic peritonitis. As previously discussed, Applicants have surprisingly discovered that testing for peptidoglycans can be effectively utilized to prevent peritonitis due to peptidoglycan contamination where Applicants have conducted investigations that demonstrate the correlation between peptidoglycan and aseptic peritonitis and further have demonstrated that peptidoglycan in an amount of about 10 ng/mL or less can be present in the peritoneal dialysis solution without causing peritonitis due to peptidoglycan contamination.

Moreover, nowhere does the cited art teach or suggest that testing for peptidoglycan (e.g., SLP test) in addition to acidophilic thermophilic bacteria (modified bioburden test) associated with the glucose polymer can be used as a screening tool to determine whether a solution that

contains the glucose polymer can be made at peptidoglycan levels that do not exceed the threshold level of 10 ng/mL and further whether the solution is sterile. Clearly, this contrasts the claimed invention as further supported in the specification and discussed above.

Again, Applicants have recognized that acidophilic thermophilic bacteria were undetectable under current Pharmacopoeia standards due to the underlying conditions being used. The inventors determined that bioburden testing under modified conditions can be effectively utilized to detect acidophilic thermophilic bacteria and further use same in addition to peptidoglycan testing (e.g., SLP test) as a screening tool to produce a safe and effective peritoneal dialysis solution. See, Specification, page 19, line 25 to page 20, line 2. Therefore, Applicants do not believe that one skilled in the art would be inclined to modify the combined teachings of the cited references to cover the claimed invention. What the Patent Office has done is to rely on hindsight reasoning to justify the combination and modification of the references in support of the obviousness rejection. This is improper, and thus, the obviousness rejection should be withdrawn in view of same.

Applicants are submitting herewith a Supplemental Information Disclosure Statement. Applicants respectfully request that the references identified in the Supplemental Information Disclosure Statement be considered for examination purposes and further submit that the claimed invention is patentable over the cited art identified therein.

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration of same.

Respectfully submitted,

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